



IPW

PATENT  
Customer No. 22,852  
Attorney Docket No. 08702.0128-00000

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of: )  
WOLFMAN et al. ) Group Art Unit: 1652  
Application No.: 10/662,438 ) Confirmation No.: 2654  
Filed: September 16, 2003 ) Examiner: Ramirez, Delia M.  
For: METALLOPROTEASE ACTIVATION OF )  
MYOSTATIN, AND METHODS OF )  
MODULATING MYOSTATIN ACTIVITY )

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**THIRD SUPPLEMENTAL**

**INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. § 1.97(b)**

Pursuant to 37 C.F.R. §§ 1.56 and 1.97(b), Applicants bring to the attention of the Examiner the documents on the attached listing. This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits for the above-referenced application.

Copies of the listed foreign and non-patent literature documents are attached.

Copies of the U.S. patent publications are not enclosed.

Applicants respectfully request that the Examiner consider the listed documents and indicate that they were considered by making appropriate notations on the attached form.

Applicants include these references because they were cited in other GDF-8 applications assigned to Wyeth, Applicants' assignee. Applicants have not considered

PATENT  
Customer No. 22,852  
Attorney Docket No. 08702.0128-00000

or characterized these references, but are simply submitting them for the Examiner's consideration.

Applicants will continue to submit all documents that are material to patentability as they become aware of them.

This submission does not represent that a search has been made or that no better art exists and does not constitute an admission that each or all of the listed documents are material or constitute "prior art." If the Examiner applies any of the documents as prior art against any claim in the application and Applicants determine that the cited documents do not constitute "prior art" under United States law, Applicants reserve the right to present to the office the relevant facts and law regarding the appropriate status of such documents.

Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of the documents be applied against the claims of the present application.

If there is any fee due in connection with the filing of this Statement, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

Dated: June 17, 2005

By: Mary K. Ferguson  
Mary K. Ferguson  
Reg. No. 51,675

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet

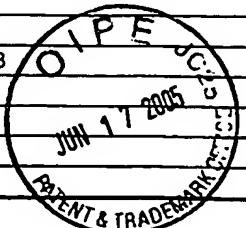
1

of

5

**Complete if Known**

Application Number	10/662,438
Filing Date	September 16, 2003
First Named Inventor	Wolfman, et al.
Art Unit	1652
Examiner Name	Ramierz, Delia M.
Attorney Docket Number	08702.0128-00000

**U.S. PATENTS AND PUBLISHED U.S. PATENT APPLICATIONS**

Examiner Initials	Cite No. <sup>1</sup>	Document Number	Issue or Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code <sup>2</sup> (if known)			
		5,639,638	06-17-1997	Wozney et al.	
		5,700,911	12-23-1997	Wozney et al.	
		5,723,125	03-03-1998	Chang et al.	
		5,756,457	05-26-1998	Wang et al.	
		5,827,733	10-27-1998	Lee et al.	
		5,914,234	06-22-1999	Lee et al.	
		6,004,937	12-21-1999	Wood et al.	
		6,096,506	08-01-2000	Lee et al.	
		6,340,668	01-22-2002	Celeste et al.	
		6,368,597	04-09-2002	Strassmann et al.	
		6,369,201	04-09-2002	Barker et al.	
		6,437,111	08-20-2002	Wozney et al.	
		6,656,475	12-02-2003	Lee et al.	
		6,696,260	02-24-2004	Lee et al.	
		6,835,544	12-28-2004	Mathews et al.	
		US-2002-0150577 A1	10-17-2002	Lee et al.	
		US-2003-0138422 A1	07-24-2003	Aghajanian et al.	
		US-2003-0162714 A1	08-28-2003	Hill et al.	
		US-2003-0180306 A1	09-25-2003	Hill et al.	
		US-2004-0077053 A1	04-22-2004	Lee et al.	
		US-2004-0142382 A1	07-22-2004	Veldman et al.	
		US-2004-0181033 A1	09-16-2004	Han et al.	
		US-2004-0223966 A1	11-11-2004	Wolfman et al.	

Note: Submission of copies of U.S. Patents and published U.S. Patent Applications is not required.

**FOREIGN PATENT DOCUMENTS**

Examiner Initials	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Translation <sup>6</sup>
		Country Code <sup>3</sup> Number <sup>4</sup> Kind Code <sup>5</sup> (if known)				
		EP 1 061 940 B1	12-17-2003	Genetics Institute LLC		
		EP 1 444 985 A2	08-11-2004	Genetics Institute LLC		
		WO 94-21681	09-29-1994	Johns Hopkins University School of Medicine		
		WO 94-26892	11-24-1994	Genetics Institute, Inc.		
		WO 96-01845	01-25-1996	The Johns Hopkins University School of Medicine		

**Complete if Known**

<i>Application Number</i>	10/662,438
<i>Filing Date</i>	September 16, 2003
<i>First Named Inventor</i>	Wolfman, et al.
<i>Art Unit</i>	1652
<i>Examiner Name</i>	Ramierz, Delia M.

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet

2

of

5

Attorney Docket Number

08702.0128-00000

**FOREIGN PATENT DOCUMENTS**

	WO 99-24058	05-20-1999	Genetics Institute, Inc.		
	WO 99-45949	09-16-1999	Genetics Institute, Inc.		
	WO 99-56768	11-11-1999	Metamorphix, Inc.		
	WO 00-11163	03-02-2000	Regeneron Pharmaceuticals, Inc.		
	WO 00-43781	07-27-2000	Metamorphix Inc.		
	WO 01-64888 A2	09-07-2001	Zymogenetics, Inc		
	WO 02-068650 A2	09-06-2002	Wyeth		
	WO 02-09641 A2	02-07-2002	The Johns Hopkins University School of Medicine		
	WO 03-027248	04-03-2003	Wyeth		
	WO 04-058988 A2	07-15-2004	Amgen, Inc.		

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation <sup>6</sup>
		Alexander et al., "Human Parathyroid Hormone 1-34 Reverses Bone Loss In Ovariectomized Mice," <i>J. Bone Miner. Res.</i> 16:1665-1673 (2001)	
		Alliel et al., "Testican, a Multidomain Testicular Proteoglycan Resembling Modulators of Cell Social Behaviour," <i>Eur. J. Biochem.</i> 214:347-350 (1993)	
		Amthor et al., "The Expression and Regulation of Follistatin and a Follistatin-like Gene During Avian Somite Compartmentalization and Myogenesis," <i>Dev. Biol.</i> 178:343-362 (1996)	
		Andersson et al., "Repeated <i>In Vivo</i> Determinations of Bone Mineral Density During Parathyroid Hormone Treatment in Ovariectomized Mice," <i>J. Endocrinol.</i> 170:529-537 (2001)	
		Ashmore et al., "Comparative Aspects of Muscle Fiber Types in Fetuses of the Normal and "Double-Muscled" Cattle," <i>Growth</i> 38:501-506 (1974)	
		Attisano et al., "Activation of Signalling by the Activin Receptor Complex," <i>Mol. Cell. Biol.</i> 16:1066-1073 (1996)	
		Bakker et al., Duchenne and Becker Muscular Dystrophies. In <i>Diagnostic Criteria for Neuromuscular Disorders</i> , 2nd ed., Emery, ed., Royal Society of Medicine Press, 1998; pp 1-4	
		Bartholin et al., "FLRG, an Activin-Binding Protein, is a New Target of TGF $\beta$ Transcription Activation Through Smad Proteins," <i>Oncogene</i> 20:5409-5419 (2001)	
		Brown et al., "Physicochemical Activation of Recombinant Latent Transforming Growth Factor-beta's 1, 2, and 3," <i>Growth Factors</i> 3:35-43 (1990)	
		Bulfield et al., "X Chromosome-Linked Muscular Dystrophy ( <i>mdx</i> ) in the Mouse," <i>Proc. Natl. Acad. Sci. U.S.A.</i> 81:1189-1192 (1984)	
		Derynck et al., "Human Transforming Growth Factor- $\beta$ Complementary DNA Sequence and Expression in Normal and Transformed Cells," <i>Nature</i> 316:701-705 (1985)	

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(Use as many sheets as necessary)</i>				<b>Complete if Known</b>	
Sheet	3	of	5	<i>Application Number</i>	10/662,438
				<i>Filing Date</i>	September 16, 2003
				<i>First Named Inventor</i>	Wolfman, et al.
				<i>Art Unit</i>	1652
				<i>Examiner Name</i>	Ramierz, Delia M.
				<i>Attorney Docket Number</i>	08702.0128-00000

<b>NON PATENT LITERATURE DOCUMENTS</b>					
		Emery, "The Muscular Dystrophies," <i>Lancet</i> 359:687-695 (2002)			
		Escolar et al., "Pharmacologic and Genetic Therapy for Childhood Muscular Dystrophies," <i>Current Neurology and Neuroscience Reports</i> 1:168-174 (2001)			
		Gamer et al., "A Novel BMP Expressed in Developing Mouse Limb, Spinal Cord, and Tail Bud Is a Potent Mesoderm Inducer in <i>Xenopus</i> Embryos," <i>Dev. Biol.</i> 208:222-232 (1999)			
		Gamer et al., "Gdf11 is a Negative Regulator of Chondrogenesis and Myogenesis in the Developing Chick Limb," <i>Dev. Biol.</i> 229:407-420 (2001)			
		Gentry et al., "The Pro Domain of Pre-Pro-Transforming Growth Factor $\beta$ 1 When Independently Expressed Is a Functional Binding Protein for the Mature Growth Factor," <i>Biochemistry</i> 29:6851-6857 (1990)			
		Gillis, "Multivariate Evaluation of the Functional Recovery Obtained by the Overexpression of Utrophin in Skeletal Muscles of the <i>mdx</i> Mouse," <i>Neuromuscular Disorders</i> 12:S90-S94 (2002)			
		Grady et al., "Skeletal and Cardiac Myopathies in Mice Lacking Utrophin and Dystrophin: A Model for Duchenne Muscular Dystrophy," <i>Cell</i> 90:729-738 (1997)			
		Granchelli et al., "Pre-Clinical Screening of Drugs Using the <i>mdx</i> Mouse," <i>Neuromuscular Disorders</i> 10:235-239 (2000)			
		Hamrick et al., "Bone Mineral Content and Density in the Humerus of Adult Myostatin-Deficient Mice," <i>Calcif. Tissue Int.</i> 71(1):63-68 (2002)			
		Hamrick et al., "Femoral Morphology and Cross-Sectional Geometry of Adult Myostatin-Deficient Mice," <i>Bone</i> 27:343-349 (2000)			
		Hayette et al., "FLRG (Follistatin-Related Gene), A New Target of Chromosomal Rearrangement in Malignant Blood Disorders," <i>Oncogene</i> 16:2949-2954 (1998)			
		Hoffman et al., "Conservation of the Duchenne Muscular Dystrophy Gene in Mice and Humans," <i>Science</i> 238:347-350 (1987)			
		Hoodless et al., "Mechanisms and Function of Signaling by the TGF $\beta$ Superfamily," <i>Curr. Top. Microbiol. Immunol.</i> 228:236-272 (1998)			
		Jiang et al., "Characterization and Identification of the Inhibitory Domain of GDF-8 Propeptide," <i>Biochem. Biophys. Res. Commun.</i> 315:525-531 (2004)			
		Kambadur et al., "Mutations in <i>myostatin</i> (GDF8) In Double-Muscled Belgian Blue and Piedmontese Cattle," <i>Genome Res.</i> 7:910-915 (1997)			
		Kato, "A Secreted Tumor-Suppressor, mac25, with Activin-Binding Activity," <i>Mol. Med.</i> 6:126-135 (2000)			
		Khurana et al., "Pharmacological Strategies for Muscular Dystrophy," <i>Nature Rev. Drug Disc.</i> 2:379-386 (2003)			
		Kim et al., "Inhibition of Preadipocyte Differentiation by Myostatin Treatment in 3T3-L1 Cultures," <i>Biochem. Biophys. Res. Commun.</i> 281:902-906 (2001)			
		Kingsley, D.M., "The TGF- $\beta$ Superfamily: New Members, New Receptors, and New Genetic Tests of Function in Different Organisms," <i>Genes Dev.</i> 8:133-146 (1994)			
		Lang et al., "Regulation of Myostatin by Glucocorticoids After Thermal Injury," <i>FASEB J.</i> 15:1807-1809 (2001)			
		Lin et al., "Expression Cloning of the TGF- $\beta$ Type II Receptor, a Functional Transmembrane Serine/Threonine Kinase," <i>Cell</i> 68:775-785 (1992)			

**Complete if Known**

Sheet

4

of

5

Application Number 10/662,438

Filing Date September 16, 2003

First Named Inventor Wolfman, et al.

Art Unit 1652

Examiner Name Ramierz, Delia M.

Attorney Docket Number 08702.0128-00000

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

**Complete if Known**

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(Use as many sheets as necessary)</i>			
Sheet	5	of	5
		<i>Attorney Docket Number</i>	
		08702.0128-00000	

**NON PATENT LITERATURE DOCUMENTS**

	Schäcke et al., "Mechanisms Involved in the Side Effects of Glucocorticoids," <i>Pharmacol. Ther.</i> 96:23-43 (2002)	
	Schneyer et al., "Follistatin-Related Protein (FSRP): A New Member of the Follistatin Gene Family," <i>Mol. Cell. Endocrinol.</i> 180:33-38 (2001)	
	Shibamura et al., "Cloning From a Mouse Osteoblastic Cell Line of a Set of Transforming-Growth-Factor-β1-Regulated Genes, One of Which Seems to Encode a Follistatin-Related Polypeptide," <i>Eur. J. Biochem.</i> 217:13-19 (1993)	
	Swatland et al., "Fetal Development of the Double Muscled Condition in Cattle," <i>J. Anim. Sci.</i> 38:752-757 (1974)	
	Torres et al., "The Mutant mdx: Inherited Myopathy in the Mouse," <i>Brain</i> 110:269-299 (1987)	
	Trexler et al., "Distinct Expression Pattern of Two Related Human Proteins Containing Multiple Types of Protease-Inhibitory Modules," <i>Biol. Chem.</i> 383:223-228 (2002)	
	Trexler et al., "A Human Protein Containing Multiple Types of Protease-Inhibitory Modules," <i>Proc. Natl. Acad. Sci. U.S.A.</i> 98:3705-3709 (2001)	
	Tsuchida et al., "Identification and Characterization of a Novel Follistatin-like Protein as a Binding Protein for the TGF-β Family," <i>J. Biol. Chem.</i> 275:40788-40796 (2000)	
	Tsuchida et al., "Intracellular and Extracellular Control of Activin Function by Novel Regulatory Molecules," <i>Mol. Cell. Endocrinol.</i> 180:25-31 (2001)	
	Umland et al., "Review of the Molecular and Cellular Mechanisms of Action of Glucocorticoids for Use in Asthma," <i>Pulmonary Pharmacology &amp; Therapeutics</i> 15:35-50 (2002)	
	Wakefield et al., "Latent Transforming Growth Factor-β From Human Platelets," <i>J. Biol. Chem.</i> 263:7646-7654 (1988)	
	Wu et al., "Autoregulation of Neurogenesis by GDF-11," <i>Neuron</i> 37:197-207 (2003)	
	Wuytens et al., "Identification of Two Amino Acids in Activin A That Are Important for Biological Activity and Binding to the Activin Type II Receptors," <i>J. Biol. Chem.</i> 274:9821-9827 (1999)	
	Zhu et al., "Dominant Negative Myostatin Produces Hypertrophy without Hyperplasia in Muscle," <i>FEBS Lett.</i> 474:71-75 (2000)	
	Zwusen et al., "Characterization of a Rat C <sub>6</sub> Glioma-Secreted Follistain-Related Protein (FRP) Cloning and Sequence of the Human Homologue," <i>Eur. J. Biochem.</i> 225:937-946 (1994)	

Examiner Signature	Date Considered	
--------------------	-----------------	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.